



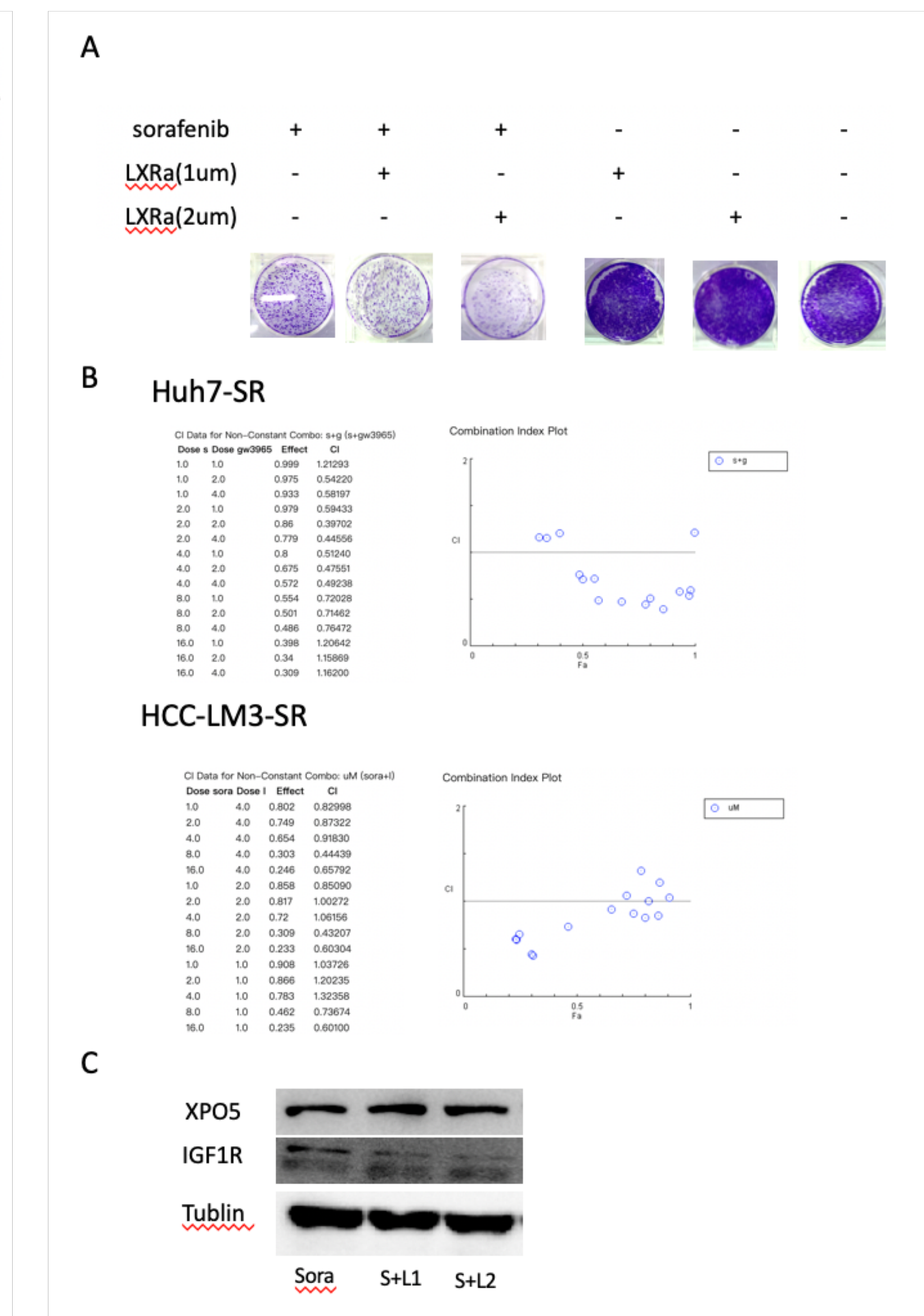
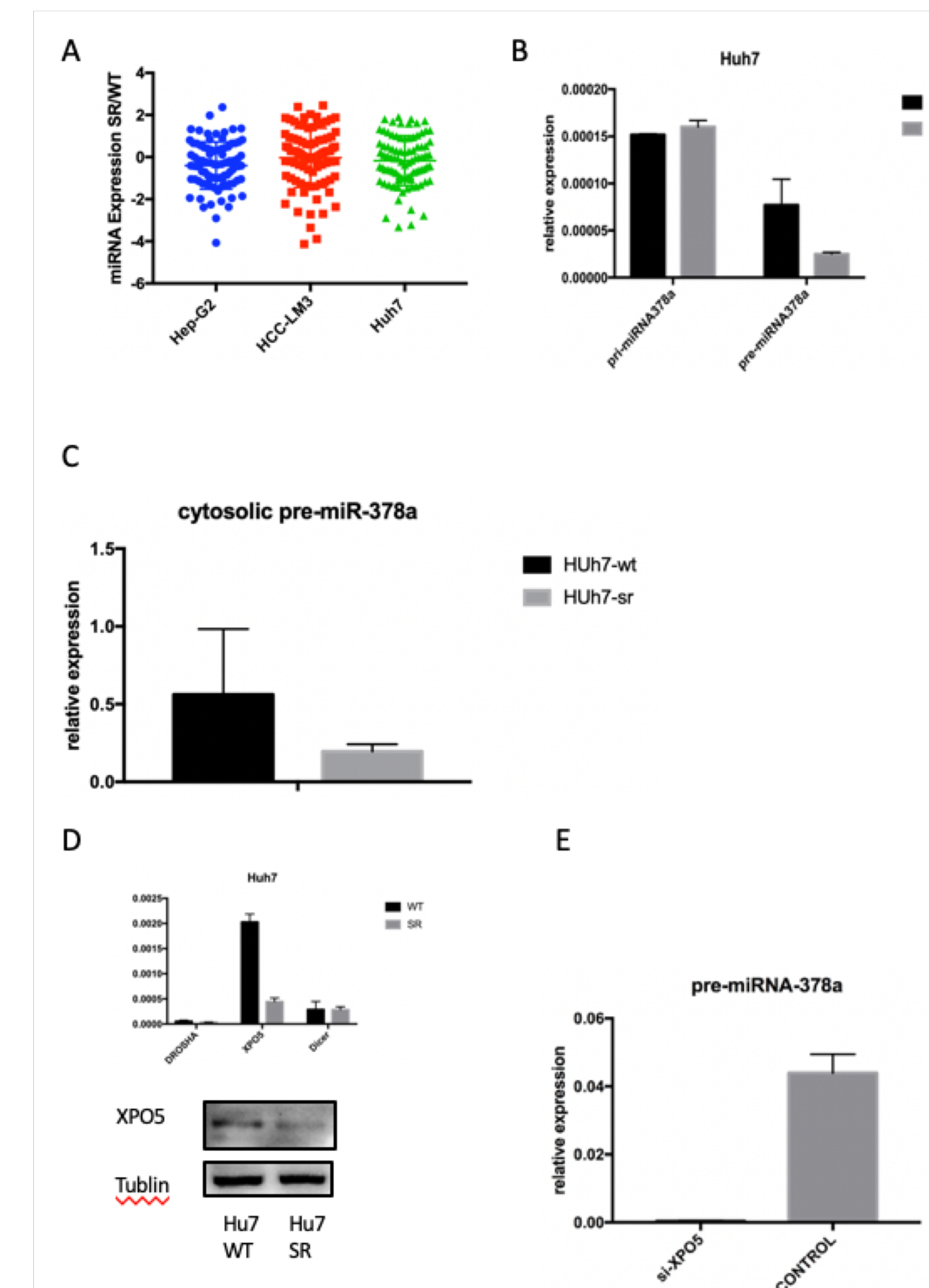
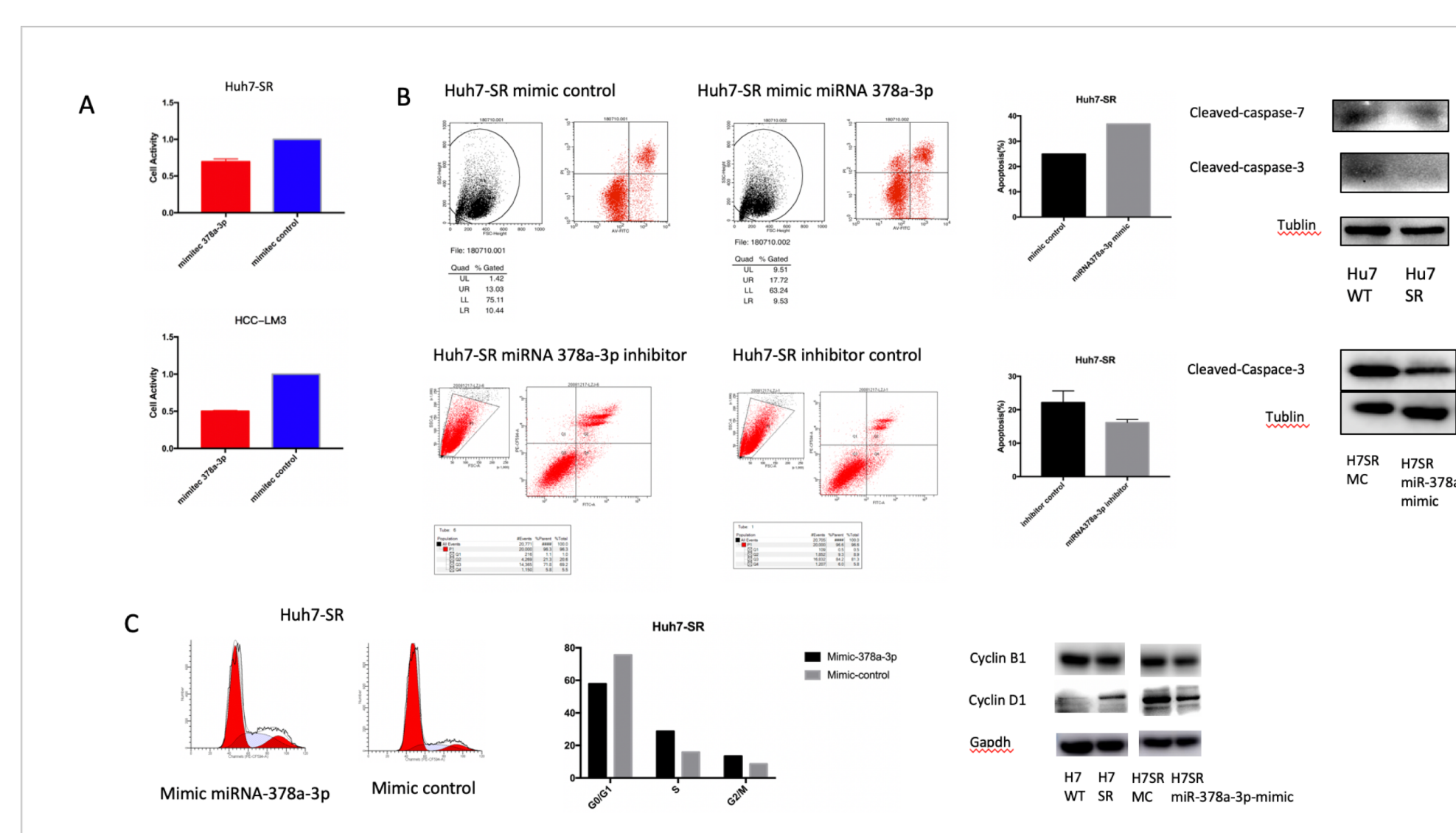
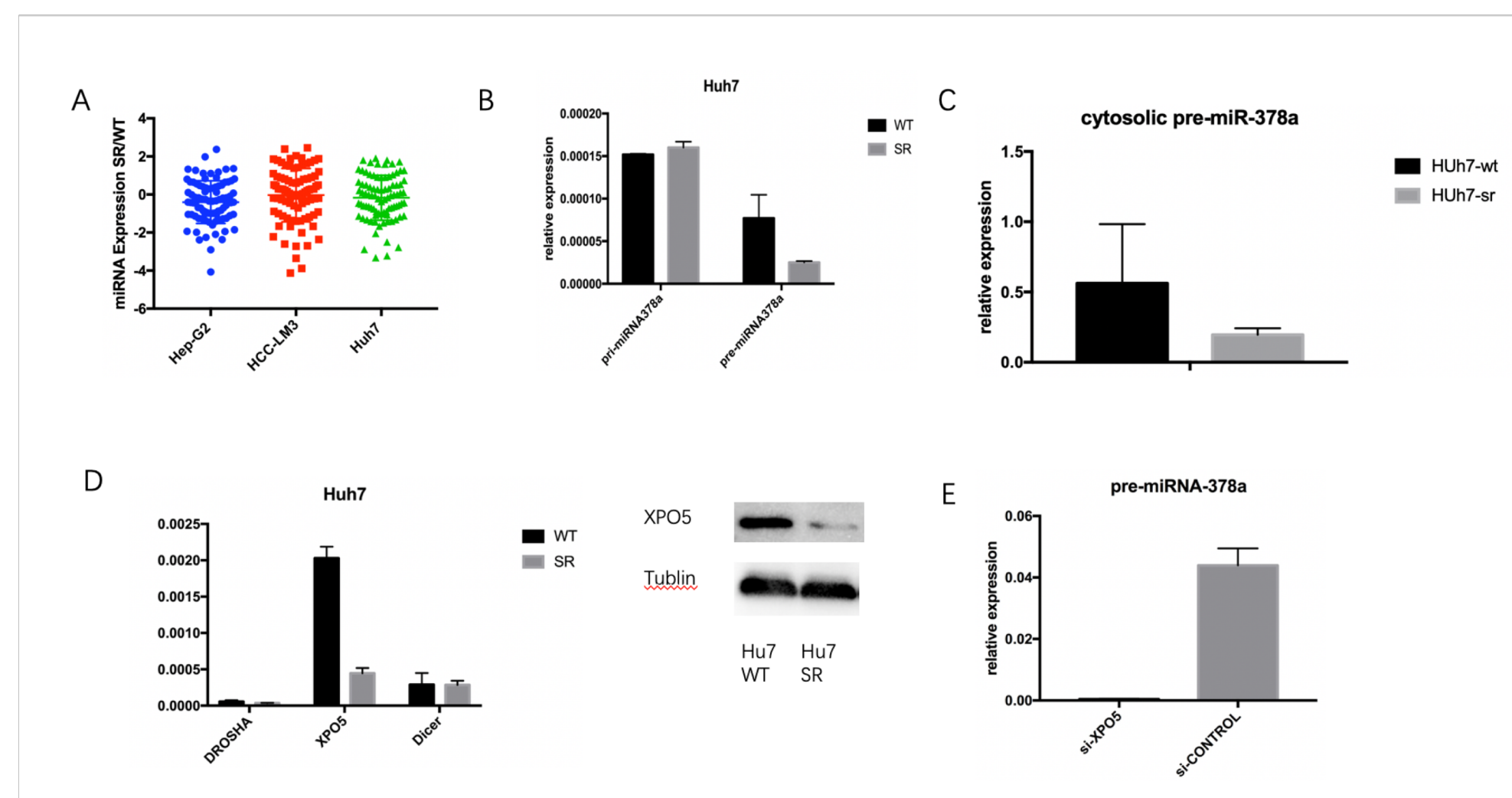
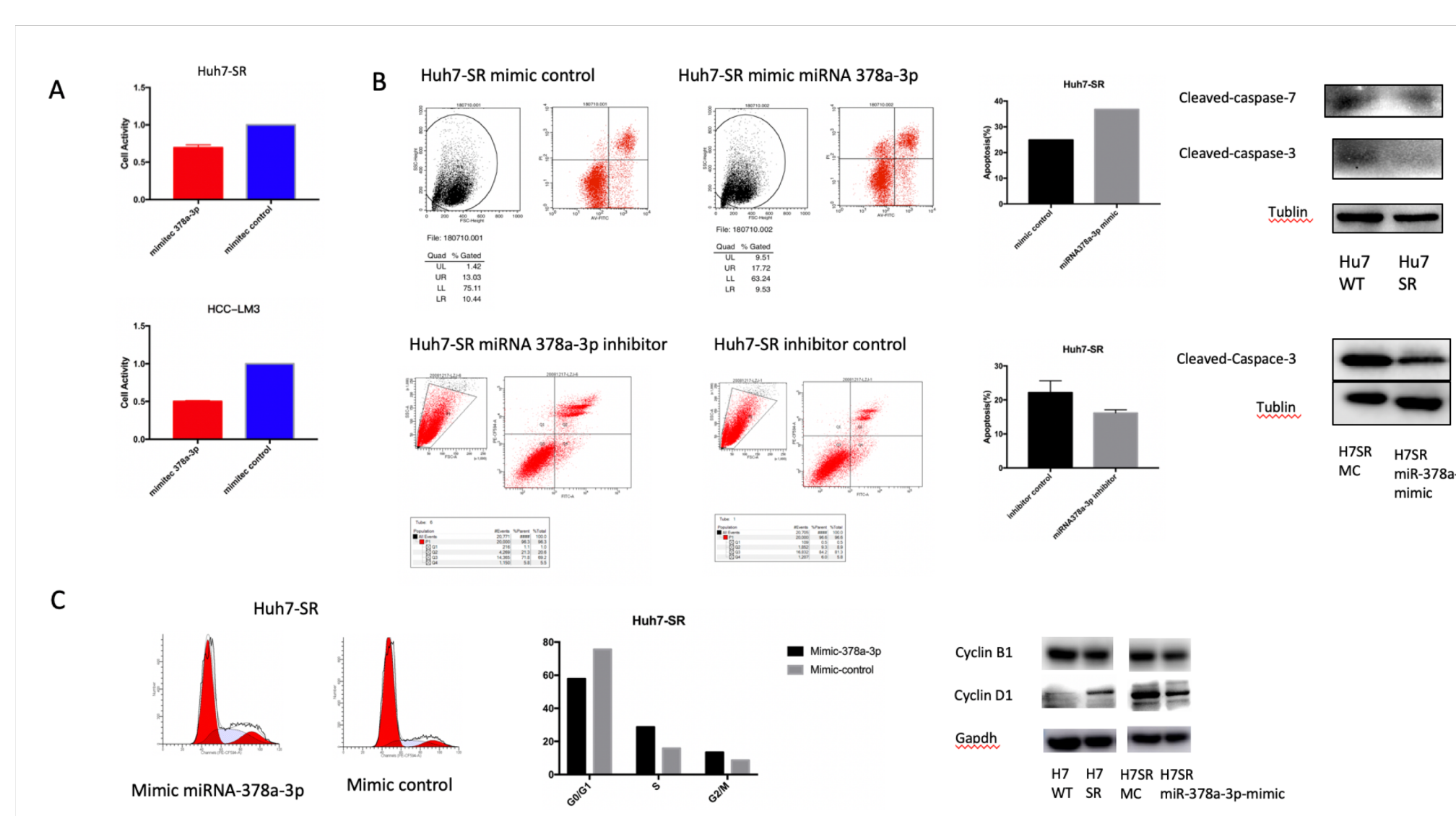
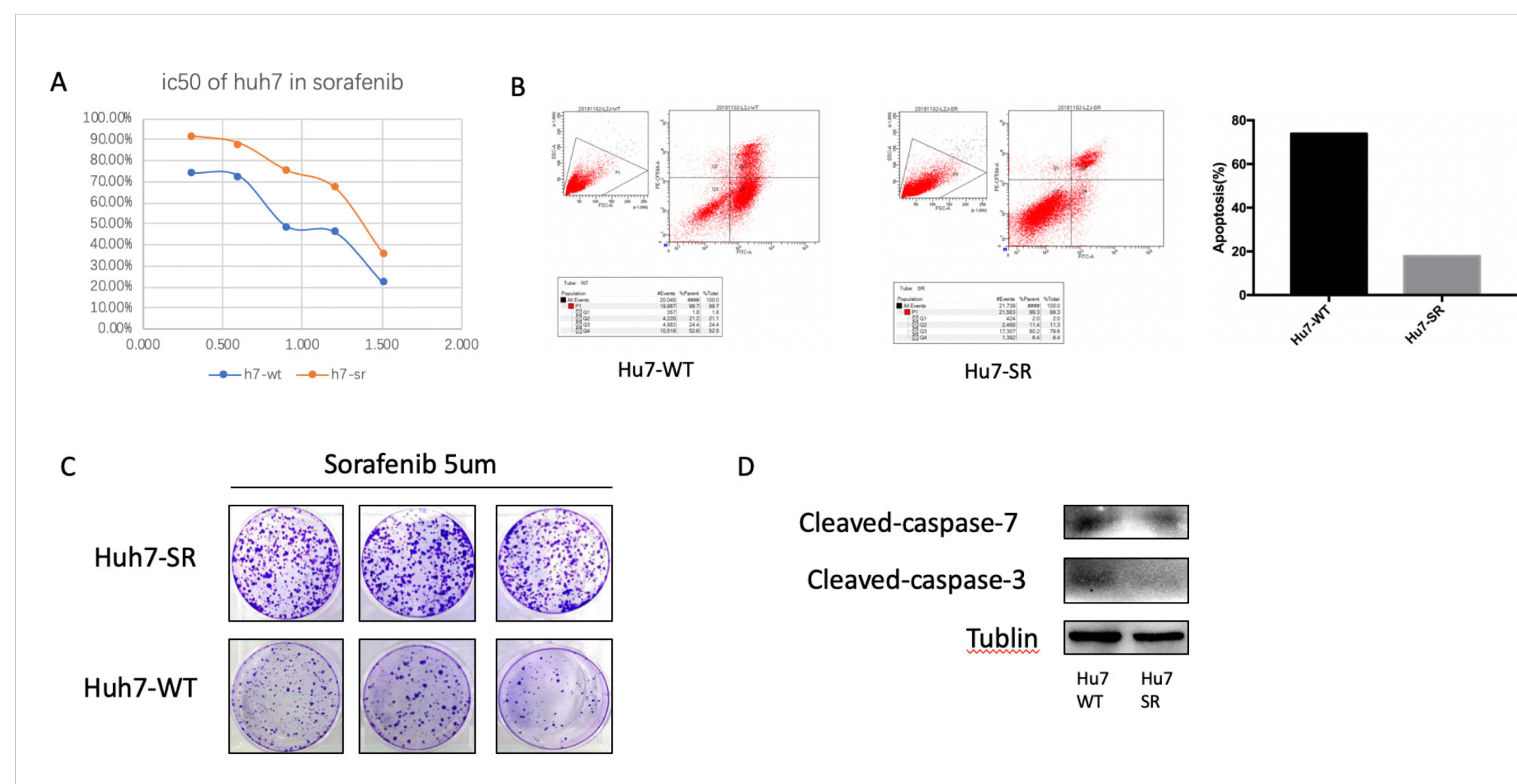
INTRODUCTION

Sorafenib is the first-line treatment for advanced hepatocellular carcinoma (HCC), but the clinical response to sorafenib is seriously limited by drug resistance. Dysregulation of microRNA play a critical roles in sorafenib resistance.

AIM

Our studies have a better understanding of the dysfunction of microRNA in the sorafenib resistance in HCC cells.

RESULTS



METHOD

We used fluorescence in situ hybridization, separation of nuclear and cytoplasmic fractions, quantitative reverse transcription PCR to study the locality of the precursor microRNA-378a. CRISPR/cas9, immunohistochemistry, luciferase assays and immunoblotting to study the role of miR-378a in sorafenib resistance cell. Patient-derived xenografts and cell-derived xenografts were used to study the functions of microRNA-378a.

CONCLUSIONS

Attenuated XPO5-mediated export of precursor-miRNA limitation conferred sorafenib resistance in HCC. GW3965 treatment (LXRα agonist) in combination with sorafenib represents a novel therapeutic strategy for HCC treatment.

REFERENCES

- 1.Sun HL, Cui R, Zhou J, et al. ERK Activation Globally Downregulates miRNAs through Phosphorylating Exportin-5. *Cancer Cell*. 2016;30(5):723-736
- 2.Wu K, He J, Pu W, Peng Y. The Role of Exportin-5 in MicroRNA Biogenesis and Cancer. *Genomics Proteomics Bioinformatics*. 2018;16(2):120-126
- 3.Zhang T, Duan J, Zhang L, et al. LXRα Promotes Hepatosteatosis in Part Through Activation of MicroRNA-378 Transcription and Inhibition of Ppargc1β Expression. *Hepatology*. 2018
- 4.Chang H, Yi B, Ma R, Zhang X, Zhao H, Xi Y. CRISPR/cas9, a novel genomic tool to knock down microRNA in vitro and in vivo. *Sci Rep*. 2016

ACKNOWLEDGEMENTS

This study was supported by grants by Natural Science Foundation of Zhejiang Province (CN) (grant no. LY15H160030 and no. LY15H160031) and Chinese Medicine Research Program of Zhejiang Province (CN) (grant no. 2012ZA087).

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